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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/920,879	08/02/2001	David Y. Chien	CHIR-0316	5787

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EXAMINER	
HUMPHREY, LOUISE WANG ZHIYING	
ART UNIT	PAPER NUMBER
1648	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/920,879	CHIEN, DAVID Y.	
	Examiner	Art Unit	
	Louise Humphrey, Ph.D.	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 July 2007 and 15 October 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11,19-27 and 30-33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11,19-27 and 30-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 15 October 2007 has been entered.

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

DETAILED ACTION

This Office Action is in response to the amendment filed 26 July 2007. Claims 1-10, 12-18, 28, 29 and 34-38 have been cancelled. Claims 11, 19-27 and 30-33 are pending and currently examined.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. §103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The rejection of claims 111, 19-27 and 30-33 under 35 U.S.C. §103(a) as being obvious over Ralston *et al.* (WO 92/08734; 29 May 1992) in view of Casey *et al.* (US 5,667,992) is **maintained**. Applicant's arguments have been fully considered but are not persuasive.

The instant claims are directed to a method for detecting hepatitis C virus (HCV) in a mammalian host within the first six months of HCV infection, comprising the steps of:

(a) obtaining, from the host within the first six months of HCV infection, a body component suspected of containing antibodies to HCV;

(b) contacting said body component with a purified HCV antigen, wherein said HCV antigen comprises an E1/E2 heterodimer, wherein said HCV antigen is purified under non-denaturing conditions and said contacting is performed under conditions that

allow an immunological reaction to occur, whereby detectable antibody/antigen complexes are formed; and

(c) detecting the presence of said antibody/antigen complexes, thereby detecting the presence of HCV in the mammalian host within the first six months of infection.

Ralston *et al.* teach "an immunoassay reagent" comprising an isolated HCV antigen selected from the group consisting of an antigen encoded in the E1 domain of an HCV genome, an antigen encoded in the E2 domain of an HCV genome, and aggregates thereof, wherein said HCV antigen is purified under non-denaturing (p. 4, lines 10-17; p. 6, lines 1-5; p. 12, lines 5-10; and pp. 21-22) conditions. Ralston does not expressly teach immunoassay "within the first six months of HCV infection" as claimed. That is, Ralston does not expressly teach obtaining, within the first six months of infection, a body component suspected of containing HCV antibodies, contacting the claimed isolated HCV antigen with the body component, and detecting the presence of antibody/antigen complexes, thereby detecting the presence of HCV within the host within the first six months of infection. However, Casey teaches using HCV E2 antigen in a radio-immunoprecipitation assay to screen human blood transfusion recipients for HCV antibody (col. 15, Example 3; col. 20, Table 7) by collecting serum at regular intervals and contacting with HCV E2 antigen (i.e. APP-HCV-E2) (col. 15, lines 5'4-67), which detects HCV antibodies as early as 103 days post infection (Table 7). Essentially Casey demonstrates that a skilled artisan can detect HCV in a mammalian body component using an HCV envelope antigen in less than four months post-infection.

Therefore, the Ralston immunoassay would necessarily detect HCV in mammalian body component within the first six months of HCV infection.

Regarding claim 21, Ralston does not expressly teach a kit for practicing the claimed method, including suitable vials, instructions and positive and negative controls. However, Casey teaches arranging its immunoassay reagents into a kit, including containers (col. 3, lines 11-15). Moreover, it is generally known in the art that arranging assay components into a kit ensures that all the reagents that are needed for completing the assay are present when needed. Positive and negative controls are standard components that are known to be important for proving results. Therefore, it would have been obvious to modify Ralston's reagents into a kit as taught by Casey *et al.*

Applicant argues that Ralston *et al.* fail to teach or suggest using HCV E1/E2 heterodimer in an immunoassay for HCV and that Ralston describes only the use of E1 or E2 separately in immunoassay. However, this argument mischaracterizes the reference because Ralston *et al.* disclose E1/E2 heterodimer as a species of dimers and aggregates of E1 and/or E2 (page 4, line 15-17; page 6, line 1-3) and applying the aggregate species as an immunoassay reagent (page 4, line 12-14) in a screen of a biological liquid for the presence of HCV particles (page 9, line 6-8). Ralston *et al.* also disclose a method for purifying E1:E2 complexes by expression in mammalian cells as the glycosylation of the recombinant protein should closely resemble that of the wild viral proteins (page 3, line 15-18). The recombinant E1 and E2 are expressed in

mammalian cells like HeLa and CHO cells (page 14, line17-18) with an expression vector like recombinant vaccinia virus (page 19, line 24). The recombinant proteins appear essentially identical to the envelope proteins found in the mature, free virion, or to a form of cell-associated envelope protein (page 12, line 3-11).

Applicants further argue that Casey *et al.* fail to teach or suggest using an E1/E2 heterodimer in the HCV immunoassay. However, this component is taught by Ralston *et al.*, which was applied as a primary reference. Thus, the obviousness of the combination does not hinge on whether Casey *et al.* suggest using non-denaturing conditions to preserve conformational epitopes of an E1/E2 heterodimer. Rather, the motivation to combine the references was to use the Casey publication's immunoassay timeline to show that the HCV immunoassay taught by Ralston *et al.* is able to detect HCV in a mammal within the first six months of HCV infection. Therefore, a *prima facie* case of obviousness is properly established.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Correspondence

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Louise Humphrey, Ph.D. whose telephone number is 571-272-5543. The examiner can normally be reached on Mon-Fri, 9:30 am - 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell, can be reached at 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Jeffrey Parkin, Ph.D.
Primary Examiner
02 Januay 2008

Louise Humphrey, Ph.D.
Assistant Examiner